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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/851,965	05/06/97	YOUNG	A 224/042

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EXAMINER	
CELSA, B	
ART UNIT	**PAPER NUMBER**
1627	23

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

file copy

Office Action Summary

Application No.	Applicant(s)
08/851,965	Young et al.
Examiner	**Art Unit**
Bennett Celsa	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 12, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 4-10, and 13-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-10, and 13-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *22*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 3/12/01 in paper no. 18 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/851,965 is acceptable and a CPA has been established. An action on the CPA follows.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-2, 4-10 and 13-24 are currently pending and under consideration.

Allowable Subject Matter

The following subject matter is allowable over the prior art of record:

A. A method of *treating* gastritis or gastric ulceration in a subject in need thereof by peripherally administering an amylin or an amylin agonist, wherein said amylin agonist is not a calcitonin or a CGRP; and wherein said amylin or amylin agonist has an IC50 of about 50pM or less in a rat receptor binding assay.

B. A method of *treating* or *preventing* gastritis or gastric ulceration which is induced by ethanol or a non-steroidal antiinflammatory compound (NSAID) in a *subject in need thereof* by *peripherally administering* an amylin or an amylin agonist, wherein said amylin agonist is not a

calcitonin or a CGRP; and wherein said amylin or amylin agonist has an IC50 of about 50pM or less in a rat receptor binding assay.

It is noted that the HOST in B. above removes anticipation of the prior art regarding the administration of the same class of compounds peripherally in the context of prevention.

The following is a statement of reasons for the indication of allowable subject matter: the closest prior art of record (the Guidobono references, especially the PEPTIDES 1994 reference) teach away from the peripheral administration of amylin compounds (as well as calcitonin and CGRP compounds) for treating/preventing gastritis/gastric ulcer (e..g induced by ethanol or NSAID's).

Withdrawn Objection(s) and/or Rejection(s)

In light of applicant's arguments the anticipation and obviousness rejections over the Liu et al. CN 1133718 (10/96) reference is hereby withdrawn.

Upon further consideration and in light of applicant's argument and amendment the rejection of claims 1-2, 5-10 and 13-24 under 35 U.S.C. 103(a) as being unpatentable over Evans et al., U.S. Pat. No. 4,530,838 (7/85), Gray et al, Annals of Surgery, Vol. 219 No. 1 pages 58-64, CAPLUS AN 1987:79162 to Maggi et al., Gen. Pharm. (1987) Vol. 18(1) pages 33-4 and Bates et al., Br. J. Of Pharmacology Vol. 67(3) (Nov. 1979) pages 483P-484P in view of the Specification admission as to prior art on page 6, Kolterman et al., WO 95/07098 (3/95) and WPIDS Abstract No. 98-019088 to Liu et al. CN 1133718 (10/96), taken separately or in combination is hereby withdrawn..

Upon further consideration and in light of applicant's argument and amendment the rejection of claims 1-2, 4-10 and 13 under 35 U.S.C. 103(a) as being unpatentable over Young US Pat. No. 5,677,279 (10/97), Ghyczy et al. US. Pat. No. 4,528,193, Guidobono et al., Br. J. Pharmacology and/or .Guidobono et al., Peptides is hereby withdrawn.

Upon further consideration and in light of applicant's argument and amendment the rejections over the following Guidobono references have been withdrawn:

a. The rejection of claims 1, 2, 5, 6 and 13 under 35 U.S.C. 103(a) as being unpatentable over Guidobono et al., Peptides Vol. 15 No. 4 pages 699-702 (1994)..

b. The rejection of claims 1-2, 4, 6, 9-10 and 13 under 35 U.S.C. 102(a) as being clearly anticipated by Guidobono et al., Br. J. Pharmacology Vol. 120(4) pages 581-586 (2/97)..

c. The rejection of claims 1-2, 4-6, 9-10 and 13 under 35 U.S.C. 103(a) as being unpatentable over Guidobono et al., Br. J. Pharmacology Vol. 120(4) pages 581-586 (2/97)

Upon further consideration and in light of applicant's argument and amendment, the rejection of claims 1-2, 4-10, 13-16 and 19-24 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification clearly discloses differences between "amylin agonists" such as CGRP and calcitonin and further discloses the Guidobono reference(s) thus providing possession of embodiments (calcitonins and CGRP compounds) which can be later excluded without constituting new matter (e.g. distinguishes over the *Grasselli* case).

New (or Modified) Objection (s) and/or Rejection (s)

3. Claims 1-2, 5-8, 13, 15-16 and 20-24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kolterman et al., WO 95/07098 (3/95)..

Kolterman et al. disclose the *peripheral* administration of "amylin" or "amylin agonists", especially "amylin agonist analogues" which are preferred (e.g. see pages 29-30) and tri-pro h-amylin which is most preferred (see tripro 25,28,29 human amylin, AKA AC-0137: See e.g. page 21 under "Summary of the Invention") for reducing gastric motility and slowing gastric emptying (e.g. See Abstract and PCT claims). In a preferred embodiment, AC-O137 is administered to humans (e.g. by placebo, infusion or by an IV bolus) over a wide range of dosages that are within the scope of the presently claimed invention. (E.g. see pages 24-25 and disclosed figures). The mode of peripheral administration (e.g. parenteral, nasal and oral: see e.g. page 42); the amounts administered (e.g. see pages 44-45) and the preferred (e.g. amylin analogues) and most preferred compounds (e.g. tri pro amylin analogues) are within the scope of the presently claimed invention. The reference generic teaching of "parenteral" administration and specifically nasal and oral administration as representative species would immediately envisage (e.g. anticipate) or alternatively render obvious other species of parenteral administration including "pulmonary", "transdermal" or "buccal" due to the limited types of other possible parenteral modalities available which would include "pulmonary", "transdermal" or "buccal"

administration. E.g. See e.g. *In re Schaumann*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978); MPEP 2131.02; MPEP 2144.08.

The actual (e.g. peripheral) administration to humans of compounds (e.g, AC-O137) in dosages within the scope of the presently claimed invention would necessarily anticipate the presently claimed invention drawn to **the prevention** of gastritis/ulcers. Additionally, the reference teaching of the administration of tri pro h-amylin to humans in amounts within the scope of the presently claimed invention directly anticipates and further anticipates (e.g. by immediately envisaging) the selection of the selection of the preferred h-amylin analogues disclosed in the reference due to the small list e.g. 20 or less (e.g. see page 29-30) and page 45 listing the top 7 amylin analogues or alternatively renders obvious the selection of the preferred amylin analogues for use in the disclosed method.

Accordingly, the reference method of reducing gastric motility and slowing gastric emptying (or any of the other reference methods) serves to inherently "prevent" or alternatively would be expected to prevent gastritis (or ulceration) because the *same peptide(s)* is applied in the *same way (e.g. administered in the same way to the same host)* in the *same amount. In re Best*, 195 USPQ 430,433 (CCPA 1977); *Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993). Thus, the reference method which performs the same method steps (e.g. administers the same drug in the same amounts to the same host) would inherently effect the same result (e.g. prevent gastritis or gastric ulceration) regardless of what "induces" the gastritis or ulceration (E.g. alcohol or NSAIDS).

Discussion

Applicant's argument directed to the above anticipation rejection over the Kolterman et al. reference was considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that the above scope of claims of the above rejections was modified to address the amended and newly added claims.

First, it is noted that applicant's arguments directed toward treatment (e.g. patient must have the condition) is not responsive to the above anticipation rejection.

Secondly, applicant argues that to prevent gastritis a subject must be "at risk for gastritis" which is not convincing for the following reasons.

First, the argument is not commensurate in scope to the claimed invention which is not limited to "at risk" subjects. Secondly, even if the claimed invention was so limited, applicant has failed to demonstrate that the Kolterman subjects which include subjects undergoing gastrointestinal procedures and who have gastrointestinal disorders (e.g. see Kolterman claims) would not be within those subjects "at risk" of developing gastritis.

Applicant further argues (e.g. by citing case law) that inherency requires a certainty of the result.

However, a reference which meets applicant's exact method steps e.g. teaches the peripheral administration of a specific peptide(s) (e.g. amylin or "agonists" thereof) to a subject in amounts and by modes of administration *which are clearly within the scope of the presently*

claimed invention would engender more than a mere probability, but indeed a certainty of inherently achieving the same result.

Applicant again is failing to address the crux of the above anticipation rejection e.g. whether the same administration of the same pharmacological agent (e.g. amylin or "agonists" thereof) in the same amounts the same "subject" (e.g. **any patient (e.g. the Kolterman patient)** would *necessarily* INHERENTLY achieve the same "preventive" effect (e.g. prevent gastritis or ulceration) as presently claimed. An affirmative answer to this question is inevitable; especially in the present instance since the reference is clearly targeting the same area of the body (e.g. the stomach) as in the presently claimed invention.

Accordingly, the above rejection is hereby retained.

4. Claims 14, 18 and 19 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kolterman et al. WO 95/07098 (3/95) alone and further in view of the specification to demonstrate inherency. E.g. See MPEP 2131.01(d) permits the citation of references or extrinsic evidence in an anticipation rejection under 35 U.S.C. 102, including applicant's own specification (e.g. see , *Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993).

Kolterman et al. disclose the *peripheral* administration of "amylin" or "amylin agonists", especially "amylin agonist analogues" which are preferred (e.g. see pages 29-30) and tri-pro h-amylin which is most preferred (see tripro 25,28,29 human amylin, AKA AC-0137: See e.g.

page 21 under "Summary of the Invention") for reducing gastric motility and slowing gastric emptying (e.g. See Abstract and PCT claims).

It is also noted that Kolterman teaches the use of amylin agonists which INHERENTLY possess IC 50's within the scope of the presently claimed invention (e.g. 50pM or less) such as tripro 25,28,29 as well as other amylin analogues (e.g. see Kolterman page 45, bottom paragraph) including 18Arg25,28Pro-h amylin. **See present specification at pages 36 (bottom) and page 37 (Table).**

In a preferred embodiment, AC-O137 is administered to humans (e.g. by placebo, infusion or by an IV bolus) over a wide range of dosages that are within the scope of the presently claimed invention. (E.g. see pages 24-25 and disclosed figures). The mode of peripheral administration (e.g. parenteral, nasal and oral: see e.g. page 42); the amounts administered (e.g. see pages 44-45) and the preferred (e.g. amylin analogues) and most preferred compounds (e.g. tri pro amylin analogues) are within the scope of the presently claimed invention. The reference generic teaching of "parenteral" administration and specifically nasal and oral administration as representative species would immediately envisage (e.g. anticipate) or alternatively render obvious other species of parenteral administration including "pulmonary", "transdermal" or "buccal" due to the limited types of other possible parenteral modalities available which would include "pulmonary", "transdermal" or "buccal" administration. E.g. See e.g. *In re Schaumann*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978); MPEP 2131.02; MPEP 2144.08.

The actual (e.g. peripheral) administration to humans of compounds (e,g, AC-O137) in dosages within the scope of the presently claimed invention would necessarily anticipate the presently claimed invention drawn to **the prevention** of gastritis/ulcers. Additionally, the reference teaching of the administration of tri pro h-amylin to humans in amounts within the scope of the presently claimed invention directly anticipates and further anticipates (e.g. by immediately envisaging) the selection of the selection of the preferred h-amylin analogues disclosed in the reference due to the small list e.g. 20 or less (e.g. see page 29-30) and page 45 listing the top 7 amylin analogues or alternatively renders obvious the selection of the preferred amylin analogues for use in the disclosed method.

Accordingly, the reference method of reducing gastric motility and slowing gastric emptying (or any of the other reference methods) serves to inherently "prevent" or alternatively would be expected to prevent gastritis (or ulceration) because the *same peptide(s)* is applied in the *same way (e.g. administered in the same way to the same host)* in the *same amount*. *In re Best*, 195 USPQ 430,433 (CCPA 1977); *Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993).

Accordingly the reference method which performs the same method steps (e.g. administers the same drug in the same amounts to the same host) would inherently effect the same result (e.g. prevent gastritis or gastric ulceration) regardless of what "induces" the gastritis or ulceration (E.g. alcohol or NSAIDS).

5. Claims 1-2, 4-10, 13-16 and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In amended claim 1, the metes and bounds as to what compounds are excluded by use of the term "a CGRP" is not known. Just CGRP? Or Any CGRP "analogue" (including amylin or its analogues?).

Discussion

Applicant's arguments directed to the above indefinite rejection were considered but not deemed persuasive for the following reasons.

Applicant's case law addressing "substantially" and "close" is not on point to the presently claimed invention which lacks such terminology.

Applicant further argues that "a CGRP" would encompass the exclusion of CGRP and compounds which are "substantially CGRP" which encompasses single substitution analogues. .

This is not found persuasive since it further demonstrates the lack of a metes and bounds as to what will or will not infringe. For example, it is further unclear as to whether single substitution analogues which drastically change bioactivity are within the claimed scope ? What about addition or deletion analogues?

Accordingly, the above rejection is hereby maintained.

New Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 14 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (E.g. NEW MATTER REJECTION).

Claims 14 and 19 contain new matter since it is broadly drawn to a large genus of "amylin or amylin agonist" which possesses an "IC50" of "about 50pM (or 30pM) or less". This constitutes new matter since the specification supports the use of "purified human amylin" as possessing an IC50 of about 50pM; there is no specific support for IC50 of (30 or 50pM) or less, nor does the limited number of compound examples of specific structures provided on page 37, Table 1 provide sufficient support for the presently claimed broad generic of "amylin or amylin agonists" compounds possessing the recited IC50 values. Accordingly, to the extent that the claim reads on determining IC50 values in assays other than described and to the extent that the claim extends to amlin analogs other than those specifically described in Table 1, this added breadth constitutes new matter.

8. Claims 14, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

. Claims 14, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the specific assay and assay conditions which are "essential" for determining. IC50 value. This information is essential to enable one to know what will or will not infringe since determination of IC50 value is assay specific. Amending to recite the use of a rat receptor binding assay while pointing to the specification example relating thereto will overcome this rejection.

Claim Rejections - 35 USC § 102

9. Claims 1, 2, 5, 6, 13, 14 and 20-24 are rejected under 35 U.S.C. 102(b) as being anticipated or in the alternative obvious over Database WPI, Sec. Week 199546, AN 1995;351860 XP002163755 (1994).

AN 1995;351860 XP002163755 (1994) discloses a compositions comprising "amylin" for treating a subject (e.g. human) having gastric and duodenal ulcers (e.g gastric inflammation). Although the reference is silent as to how the chinese medicine is administered from the reference teaching one would immediately envisage (e.g. anticipate) the administration of the chinese medicine peripherally (e.g. oral) since "medicines" are rarely given to humans through the brain or spinal cord (e.g. centrally) and further in view of the limited number of art-established means of

administering medicinal compositions (e.g parenteral or enteral: including nasal/oral/pulmonary/transdermal/buccal) or in the alternative "peripheral" administration of the "amylin" containing chinese medicine would be prima facie obvious. It is noted that however, administered the chinese formulation would "inherently" prevent gastritis/ulceration since the same agent (e.g. "Amylin") is administered in the same way to the same host. IC50 values within the scope of the presently claimed invention for "amylin" represent an "inherent" property of amylin. Distinguishing this reference "amylin" from the peptidic "amylin" described in the specification will overcome this rejection. It is noted that the Examiner lacks the ability (e.g. experimental facilities) to compare the reference "amylin" to the prior art Chinese medicinal "amylin".

10. Claims 17 and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Guidobono et al. Brit. J. Pharmacol. (2/97) pages 581-586.

This Guidobono et al. reference clearly teaches that "centrally" administered "amylin" is gastroprotective (E.g. prevent/treat) toward gastric ulceration (e.g. gastritis), especially ulceration/gastritis which is induced by administering NSAIDS or ethanol. See Figures 1, 2, 4, 5 and 6 and explanations thereof. Amending to recite peripheral administration will overcome this rejection.

11. Claims 1, 2, 6, 13, 14, 17, 18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Guidobono et al. Peptides Vol. 15, No. 4 pages 699-702 (1994).

Guidobono et al. (Peptides) teaches that "periperal" (e.g. subcutaneous) and "central" administration of "amylin" to a rat (e.g a "subject ") serves to a dose-dependent fall in gastric secretion and acid concentration. E.g. see title, abstract, page 699; and page 701 left column. The reference teaching of "peripheral" administration of "amylin" to reduce gastric secretion would anticipate the use of "amylin" to PREVENT gastritis/gastric ulceration since administering the same agent (e.g. amylin) in the same amounts to the same host (e.g. a subject) in the same manner (e.g. peripherally) MUST have the presently claimed desired preventive effect (anticipating claims 1, 2, 6, 13, 14, and 23 . Similarly, the. reference teaching of "centrally" administering "amylin" to reduce gastric secretion would anticipate the use of "amylin" to PREVENT gastritis/gastric ulceration since administering the same agent (e.g. amylin) in the same amounts to the same host (e.g. a subject) in the same manner (e.g. centrally) MUST have the presently claimed desired preventive effect (anticipating claims 17 and 18 which encompasses central administration) .

12. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of *preventing/treating* gastritis or gastric ulceration induced by ethanol in a *subject in need thereof* by *peripherally or centrally administering* an amylin or an amylin agonist, wherein said amylin agonist is not a calcitonin or a

CGRP; and wherein said amylin or amylin agonist has an IC50 of about 50pM or less in a rat receptor binding assay.

the specification does not reasonably provide enablement for the use of a CGRP (or a calcitonin) for treating/preventing *ethanol-induced gastritis or gastric ulcers* via peripheral administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. .

The Maggi et al reference abstract (e.g. CAPLUS 1987: 79162: 1987) specifically teaches that the "amylin agonist" CGRP has NO anti-ulcer EFFECT on ethanol-induced gastric lesions Accordingly, the prior art (e.g. the Maggi reference) reference specifically teaches the inoperability of amylin agonist such as CGRP and presumably calcitonin (which is similar in structure and acitivty) for treating/preventing gastritis/gastric ulceration via peripheral administration.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)
June 18, 2001

BENNETT CELSA
PRIMARY EXAMINER